Simple predictors of obstructive sleep apnea in obese patients

Predictors of obstructive sleep apnea in obese patients

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Abstract
Aim: The aim of this study is to investigate BMI>30kg/m2 patients for the frequency of OSA, and to determine the effect of HS, NC, and Mp on the severity of OSA. The secondary aim is to evaluate the relationships between sleep autonomic arousal index (AAI), obesity, and OSA severity.
Material and Methods: The data were collected from 68 patients (42 male), prospectively. A Somnocheck Micro-WM94530 portable device was used to diagnose OSA. Abdominal ultrasonography (USG) was performed to evaluate the hepatosteatosis degree. The main exclusion criteria were BMI<30kg/m2, having respiratory system diseases, or comorbidities affecting the respiratory system.
Results: The percentage of OSA in evaluated obese participants was 57%. The age, NC, Mp were found to be active contributing factors for predicting OSA in obese patients (p=0.024, p=0.045, p=0.01, respectively). The respiratory-sleep disturbance measurement AAI has a positive correlation with OSA's severity in obese patients (p= 0.0001 and r= 0.414).
Discussion: The age and anthropometric evaluation (Mp and NC) in obese patients provides a quick evaluation of OSA. AAI increases with severity of OSA.In our opinion, the recorded data of sleep apnea/hypopnea index (AHI) and AAI indexes from the Somnocheck micro device could be used as a screening diagnosis method in centers where polysomnography is not available.

Keywords
OSA, Hepatosteatosis, Neck Circumference, Mallampati Score, Obesity

Introduction

Obesity is a predisposing risk factor for the development of obstructive sleep apnea (OSA). If OSA is associated with excessive daytime sleepiness, it is defined as obstructive sleep apnea syndrome (OSAS). The prevalence is 2% in females and 4% in males while it tends to be 30% in obese and 50-98% in morbidly obese people [1].

Neck circumference (NC) is more predictive of OSA than the body mass index (BMI) parameter [2]. OSAS is currently considered to be an inflammatory disorder and endothelial dysfunction in OSA is thought to be the responsible mechanism [3]. Therefore, the patients with OSA have a higher incidence of visceral obesity, and non-alcoholic fatty liver disease-hepatosteatosis (HS) than the healthy population. The patients with OSA should also be screened for the presence and the severity of HS [4].

Somnocheck Micro-WM 94530 (SC-micro) is considered as a home sleep apnea test device and also a reliable portable device in monitoring OSA patients [5]. Home sleep apnea testing (HSAT) monitoring devices, have disadvantages as well as advantages. Unlike polysomnography (PSG), they do not provide information about the stages of sleep and are not as sensitive as PSG in detecting the desaturation index and cannot record cortical sleep arousal. However, they are susceptible for detecting apnea and hypopnea index (AHI), and easy to apply and highly cost-effective [6]. The SC-micro device is capable of evaluating a volumetric finger plethysmography recording. It can demonstrate profound changes in finger pulse and pulse wave amplitude (PWA), which is determined by α-receptor-mediated changes of finger blood flow, suggesting that pulse amplitude changes reflect the capacity of the vascular endothelium under hypoxic stress [7]. In OSA evaluation, polysomnography is capable to record respiratory PWA drops during sleep and it has been shown that PWA drops occur simultaneously with EEG cortical arousal in sleep. It is estimated that PWA drop suggests a possible role of pulse wave amplitude as a marker of cerebral response to respiratory events [8]. Moreover sleep cortical arousals are generally associated with withdrawal of vagal activity and activation of the sympathetic nervous system, resulting in heart rate (HR) augmentation, vasoconstriction, and blood pressure rise. These manifestations have been indicated as autonomic arousals [9].

This study aims to determine the effect of HS, NC, and Mp in obese patients and to evaluate their influence in severity of OSA. The secondary aim is to evaluate the relationships between sleep autonomic arousal index (AAI), obesity, and OSA. Considering the fact that many patients have to wait for a very long time for PSG recordings because of limited numbers of sleep labs, we wanted to draw attention to the possible use of HSAT techniques in screening pre-PSG evaluating for diagnosis of OSA.

Material and Methods

This current study was planned to be performed from September 2019 to July 2020 in Yeditepe University hospital in obese (BMI≥30 kg/m2) patients. Ethical approval for this prospective, randomized, consecutive controlled clinical trial (number: 1120) was provided by the Yeditepe University Clinical Trials Ethical Committee, Istanbul, Turkey (Chairperson Prof T.

Celik) on 20/11/2019. The study was conducted in accordance with the Declaration of Helsinki.

The sample size of 68 was determined by the literature revealing that 27.9% of the subjects do not have OSA and 61,5% of them having BMI ≥30 kg/m2, were diagnosed with OSA within the inputs of α err prob=0.05, Power (1-β err prob) =0.80 [8]. Seventy participants were planned to be included in the study for compensation of the possible losses. Systematic random sampling was performed according to the number of patients admitted to Yeditepe University, Department of Endocrinology and Internal Medicine in Istanbul, Turkey. Participants with BMI ≥30 kg/m2 were diagnosed with obesity. The volunteers were picked among the odd-numbered ones who coded before starting the trial until they reached the sample size of 70. Written informed consent was obtained from all participants who had been assigned to the trial by the senior author.

Obese participants (BMI≥30 kg/m2) between 18-60 years of age, were chosen according to the trial eligibility criterias. Participants under the age of 18 and over the age of 60, patients with respiratory system diseases (such as; dyspnea, chronic obstructive pulmonary disease, interstitial pulmonary disease) or with comorbidities affecting the respiratory system (such as; congestive heart failure, chronic kidney disease, coronary artery disease), examined in a sleep disorder polyclinic with any respiratory symptom, and whose BMI is lower than 30 kg/m2 were planned to exclude from the study.

The participants' demographic and anthropometric data were recorded (age, height, weight, BMI, gender, and neck circumference). The Mallampati Classification assessment was evaluated as another anthropometric parameter. The participants' examination was made while the patient was sitting, the head in a neutral position, the mouth opened, and the tongue protruded maximally without phonation. Mp score was graded based on the visibility of the airway structures. Class I: The soft palate, uvula, pillars, and fauces visible; Class II: Mp pillars are not visible; Class III, soft palate can be visualized but can not in Class IV. An experienced Anesthesiology consultant evaluated Mallampati scores of the participants. Participants were then asked to complete the Epworth Sleepiness Scale (ESS) [10].

The somnographic data for the trial was obtained via a portable device, Somnocheck Micro-WM 94530 (Weinmann Medical Technology, Hamburg, Germany). This method of evaluating OSA was found to be nearly equal to polysomnography (PSG) in measuring the sleep apnea-hypopnea index (AHI), minimal and mean peripheral oxygen blood saturation (SpO2) during sleep. Participants were informed about the device and educated. The participants used the device for monitoring themselves just before bedtime at their homes. Participants who had achieved at least six hours of uninterrupted sleep were included in the study; two of the participants who had not achieved this time of uninterrupted sleeping interval or not adequately monitored themselves were excluded from the study. OSA was diagnosed by the AHI measurements recorded from the monitoring. AHI<5, AHI between 5 and 15, AHI between 15 and 30, AHI>30 were diagnosed as "simple snoring," "mild OSA," "moderate OSA," and "Severe OSA" respectively [11]. The device also measures the autonomic arousal index (AAI) via pulse wave analysis

(PWA); therefore, the AAI was also recorded and evaluated for each participant [12].

Participants were also evaluated for hepatosteatosis in the Radiology Department's ultrasonography rooms, under the same conditions of darkness by the same radiology consultant who did not know the current trial's aim. The same device and probe were used for each examination {General Electric LOGIQ E9 (CISPR11 Group 1 Class A), Wauwatosa, WI, USA,53226} (C1-5-D broad –spectrum convex transducer with bandwidth 1-6 MHz). The liver was evaluated in terms of steatosis. Hepatosteatosis has been graded visually as Grade 1: diffusely increased hepatic echogenicity, but periportal and diaphragmatic echogenicity is still appreciable. Grade 2: diffusely increased hepatic echogenicity obscuring periportal echogenicity, but diaphragmatic echogenicity is still appreciable. Grade 3: diffusely increased hepatic echogenicity obscuring periportal echogenicity and diaphragmatic echogenicity [13].

Statistical Analysis

Minimum-maximum, standard deviation, frequency, and levels evaluated from different data recorded from participants' data (categorical values) and comorbidities (number and percentage) were included in descriptive statistics. The distribution of the variables was measured by the coefficient of variation, skewness – kurtosis, histogram, detrended, and the normality test of Shapiro-Wilk. Data determined as parametric if three or more over five positivity occurred in the tests mentioned above. The age, NC, and AAI compared with the t-test of the independent sample between groups. The Mann-Whitney U test used to compare the data of the BMI, SpO2-min, and SpO2-mean groups. A Chi-square test was performed to evaluate the effect of ESS, Mp, and HS on groups. Correlations were evaluated via the Pearson Correlation test or Spearman Correlation test. SPSS 22.0 program (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) was used for the analysis. A p-value of less than 0.05 was considered to be statistically significant.

Results

Seventy participants were evaluated from September 2019 to June 2020. Two of the participants were excluded from the study. One of them was excluded due to an interrupted sleeping interval, and the other was excluded due to inadequate monitoring. Out of 68 participants involved in the trial, 29 (42,65 %) were found to have simple snoring and 39 (%57,35) cases of OSA have been found. Seventeen patients in the simple snoring group and 25 patients in the OSAS group were male,

with no significant difference between the groups (p>0.05). The mean age of participants was 42.3±9.1 years. The mean age was statistically significantly lower in patients with smple snoring (39.5±10.3) compared to those with OSAS (44.4±7.5) (p=0.024). No statistically significant difference was found between the simple snoring and OSAS groups in terms of BMI (35.5±5,2 vs 35.5±4,2, p>0.05). The mean neck circumference (NC) was statistically significantly lower in the simple snoring group (43.9±3.6 cm vs 45.8±4.1 cm, p=0.045).

When somnographic parameters were compared between the two groups; the mean AAI was significantly lower in the simple snoring group compared to the OSAS group (24.4±14 vs 30.9±12.6, p=0.049). The minimum (86,5±4,5 vs 79,7±8,1) and mean (95,0±1,5 vs 93,7±1,9) oxygen saturation values were statistically significantly higher in the simple snoring group compared to the OSAS group (p<0.001, p=0.004, respectively). BMI, NC, and sonographic parameters are also compared between OSA subgroups (Mild, Moderate, and Severe). The comparison between the OSA subgroups of "Mild vs. Moderate" and "Mild vs. Severe" were shown in Table 1. There was no significant difference between the OSA subgroups of "Moderate vs. Severe."

The categorical values, including ESS, HS score, and Mp score,

Table 2. Comparison of Simple Snoring and OSAS according to ESS, HS, and MP scores

	Simple Snoring N=29	OSAS N=39	Total N=68	p
ESS				
1(0-5): N(%)	12(41,6%)	19(48,7%)	31(45,6%)	
2(6-10): N(%)	11(37,9%)	5(12,8%)	16(23,5%)	
3(11-12): N(%)	2(6,9%)	6(15,4%)	8(11,8%)	>0,05 c
4(13-15): N(%)	2(6,9%)	6(15,4%)	8(11,8%)	
5(16-24): N(%)	2(6,9%)	3(7,7%)	5(7,4%)	
Spearman Correlation	r: 0,032			>0,05
Mallampati Score				
Mp-1 N(%)	11(37,9%)	6(15,4%)	17(25%)	
Mp-2 N(%)	12(41,4%)	16(41%)	28(41,2%)	0,01 c**
Mp-3 N(%)	2(6,9%)	15(38,5%)	17(25%)	
Mp-4 N(%)	4(13,8%)	2(5,1%)	6(8,8%)	
Spearman Correlation	r: 0,245			0,04
Hepatosteatosis Score				
HS-0 N(%)	3(11,1%)	3(9,1%)	6(10%)	
HS-1 N(%)	12(44,4%)	8(24,2%)	20(33%)	
HS-2 N(%)	7(25,9%)	10(30,3%)	17(28,3%)	>0,05 c
HS-3 N(%)	5(18,5%)	12(36,4%)	17(28,3%)	
Spearman Correlation	r: 0,222			>0,05

Table 1. Evaluation of OSAS subgroups according to BMI, Neck Circumference, and somnographic parameters

	Mild OSAS Mean±SD	Moderate OSAS Mean±SD	Severe SAS Mean±SD	Mild OSAS 95% CI of the Difference		P	Mild OSAS 95% CI of the Difference		P
				Lower	Upper		Lower	Upper	
BMI	35±3,8	35,3±5,5	36,8±3,2	-3,73	3,2	>0,05 mw	-4,82	1,18	>0,05 mw
NC	46,2±3,7	45±3,9	46±5,2	-1,78	4,09	>0,05 st	-3,34	3,66	>0,05 st
AAI	25,6±10,9	34,1±13,5	38,3±10,6	17,72	0,81	>0,05 st	-21,66	-3,65	0,008st **
SpO2-min	84,2±5,3	77±8,5	73,4±7,3	2,07	12,35	0,018 mw*	5,78	15,76	0,001 mw **
SpO2-mean	94,7±1,7	93,3±1,4	92,2±1,3	0,2	2,72	0,021 mw*	1,18	3,85	0,001 mw **

N: number of participants, SD: standard deviation, OSAS: obstructive sleep apnea syndrome, BMI: body mass index, NC: neck circumference, AAI: autonomic arousal index, SpO2: peripheral oxygen saturation mw: Mann-Whitney Test, st: Student T Test, p: p-value, *marked: p<0.05, **marked: p<0.01, ***marked: p<0.001

Table 3. Evaluation of the effect and correlation of Epworth Sleepiness Score, Mp Score, HS Score on OSAS subgroups

	Mild OSAS vs Severe OSAS		p	Moderate OSAS vs Severe OSAS		p
ESS	Mild OSAS	Severe OSAS		Moderate OSAS	Severe OSAS	
1(0-5): N(%)	11(57,9%)	2(25%)		6(54,5%)	2(25%)	
2(6-10): N(%)	2(10,5%)	2(25%)		1(9,1%)	2(25%)	
3(11-12): N(%)	4(21,1%)	1(12,5%)	>0,05ᶜ	1(9,1%)	1(12,5%)	>0,05ᶜ
4(13-15): N(%)	2(10,5%)	2(25%)		1(9,1%)	2(25%)	
5(16-24): N(%)	0	1(12,5%)		2(18,2%)	1(12,5%)	
	r: 0,032		>0,05	r: 0,193		>0,05
Mallampati Score	Mild OSAS	Severe OSAS		Moderate OSAS	Severe OSAS	
Mp-1 N(%)	5(26,3%)	1(12,5%)		0	1(12,5%)	
Mp-2 N(%)	9(47,4%)	0	0,00ᶜ***	7(63,6%)	0	0,014ᶜ**
Mp-3 N(%)	5(26,3%)	5(62,5%)		4(36,4%)	5(62,5%)	
Mp-4 N(%)	0	2(25%)		0	2(25%)	
	r: 0,515		0,006**	r: 0,487		0,034*
Hepatosteatosis Score	Mild OSAS	Severe OSAS		Moderate OSAS	Severe OSAS	
HS-0 N(%)	2(12,5%)	1(12,5%)		0	1(12,5%)	
HS-1 N(%)	6(37,5%)	1(12,5%)	>0,05ᶜ	1(12,5%)	1(12,5%)	>0,05ᶜ
HS-2 N(%)	4(25%)	2(25%)		3(37,5%)	2(25%)	
HS-3 N(%)	4(25%)	4(50%)		4(50%)	4(50%)	
	r: 0,239		>0,05	r: -0,074		>0,05

N: number of participants, OSAS:obstructive sleep apnea syndrome, Mp: mallampati Score, HS: hepatosteatosis score, ESS: epworth sleepiness score, c: Chi-square test, r: r value, p: p-value, *: p<0.05, **: p<0.01, ***: p<0.001

were compared between Simple Snoring and OSA groups. According to groups, the Spearman correlation results with r values, and the evaluation of the data were presented in Table 2. The numbers with percentages were shown in Table 3, according to the subgroups of OSA. The comparison between the OSA subgroups of "Mild vs. Severe" and "Moderate vs. Severe" were also shown in Table 3. There was no significant difference between the OSA subgroups of "Mild vs. Moderate." Pearson Correlation test revealed a significant positive correlation between AAI and AHI data, which were used for predicting simple snoring and OSA subgroups (p=0.0001 and r=0.414). AAI had a moderately significant negative correlation with SpO2-min (p=0.006 and r=0.333) but not correlated with SpO2-mean (p>0.05). Spearman's correlation test between AHI and SpO2-min, SpO2-mean data revealed a strong significant negative correlation (p=0.0001, r=0.582 and p=0.0001, r=0.514, respectively).

Discussion

The OSA-related predictiveness rate was found to be directly correlated with the highest Mp measurements. Although HS and EDSS and NC were found to be independent predictors for OSA diagnosis, their predictivity rate was found minimal. An important sleep disturbance marker that was strongly associated with severity of OSA were AAI parameters detected with PWA. It is estimated from previous trials that predictivity/sensitivity rate of PWA for the detection of an cortical EEG-micro-arousal related to a respiratory event was 89.1% [14]. Although it is not possible to detect cortical arousals on portable devices, it has been observed in recent studies that

EEGspectral analysis power density increases in almost all > 20% PWA drops even in absence of standard cortical arousal criteria and these data suggest that all PWA drops are related with subcortical brain activation that can be detected only with spectral EEG recordings [15, 16].

It is easy to diagnose OSA when the patient comes to a sleep disorder polyclinic with corresponding problems. What about obese patients who do not know that they are suffering from a sleep disorder? This current study investigates predisposing or contributing factors of OSA in obese participants who were not examined in a sleep disorder polyclinic before and usefulness of screening portable device for diagnosing of OSA in randomly selected obese subjects. Although we found that the OSA ratio in obese participants was 57,4%, there was no correlation between OSA's severity and increased BMI in obese participants. However, age, neck circumference, and Mallampatia score were the contributing factors for the diagnosis of OSA in obese participants. The Mp score was also shown to be a strong contributing factor for predicting the severity of OSA in obese participants. Soylu et al. [17] and Öztürk et al. [18] had assessed the anthropometric indexes of OSA/OSAS diagnosed patients to examine possible relationships. According to a cross-sectional study published in 2019, Mp, age, and NC's were essential factors in predicting moderate OSA, while Mp, BMI, age, and gender were more predictive in severe OSA. According to the trial, Mp was the most significant factor compared with age, BMI, and NC concerning AHI cutoffs [19]. Those findings correspond with our study, except gender and BMI, that were already high Tom et al. [20] revealed that NC measures correlate better than BMI according to AHI in BMI>30kg/m2 OSA participants. Several studies found the significant relationship between Mp and AHI [21, 22]. These findings were also in line with our study.

OSA patients are commonly known to have shorter sleep duration, short sleep latency, low sleep efficiency, and high arousal index, although the total sleep time was not different in patients without OSA. We assessed AAI, ESS, and HS grade in obese participants to examine OSA's correspondence with sleep disturbance, daytime sleepiness. Several studies were pointing out the essential co-occurrence of poor sleep quality and quantity with obesity. Weight gain and a predisposing metabolic syndrome could cause non-alcoholic fatty liver; therefore, Arısoy et al. [4] examined HS's co-occurrence with OSA and found a significant difference between the simple snoring and moderate and severe OSA groups. In this study, we did not find a significant HS grade difference between simple snoring and OSA groups. The examination of subgroups of OSA did not also reveal any difference. These findings could be explained by the BMI difference of participants who were invited to this study. In this study, all participants were obese patients, and only six of them didn show any comorbidity. A blinded radiologist evaluated 20 participants with Grade 1 HS, 17 with Grade 2 HS, and 17 with Grade 3 HS in our institute.

Daytime sleepiness was evaluated with Epworth sleepiness scale (ESS). In this study, we assess the correspondence of ESS with OSA and the severity of OSA. In clinical practice for day-time sleepiness evaluation most commonly used questionnaires are STOP, STOPBang (SB), Berlin Questionnaire (BQ), Epworth

Sleepiness Scale (ESS), and 4-Variable Screening Tool (4-V) and among them SB has been shown to have the highest predictive sensitivity (%97,6) but the lowest specitivity, ESS has shown moderate predictive specitivity (%67) [23]. According to the American Academy of Sleep Medicine Clinical Practice Guideline 4; Berlin Questionnaire, ESS, STOP Questionnaire had a low quality of evidence across AHI cutoffs.

Technically adequate Home Sleep Apnea Testing (HSAT) devices are approved for use in diagnosis of OSA. In our study obese subjects that were found with AHI >30/h on follow- up were confirmed in local sleep labs and all of them AHI values was >30/h. All patients with AHI >15/h were referred to local sleep laboratories for confirmation of the diagnosis of OSA. In practice most sleep labs recommend PSG in patients only if a single home sleep apnea test is negative, inconclusive, or technically inadequate for OSA diagnosis [4]. According to those recommendations above, we decided to use an SC-micro device with 96.2% sensitivity and 91.7% specificity of analysis in our study [18]. This device not only gives detailed AHI results but also gives Autonomous Arousal Index (AAI) results by Pulse Wave Analysis (PWA). High values of AAI are known to be associated with hypoxia. It has been shown that AAI increases could have a negative effect on sleep fragmentation. According to this current trial's AAI findings, we found a moderate negative correlation between AAI and SpO2-min and a moderate positive correlation between AAI and AHI. In line with the explanations above, this current trial reveals that increased OSA severity has a high impact on sleep AAI index values, which has a negative effect on sleep quality. Lack of waist circumference or visceral fat area measurement could be mentioned as a limitation of this trial. Another limitation could be the imbalanced number of obese patients according to gender. The last limitation that should be mentioned is using the Epworth Sleepiness Questionnaire rather than the STOP-BANG questionnaire. Although the study has some limitations, to the best of our knowledge, this is the first study that reveals AAI's correspondence with obesity and OSA.

Conclusion

The age and anthropometric evaluation (Mp and NC) in obese patients provide a quick evaluation of OSA with HSAT devices' concordance. AAI increases with OSA and the increscent severity of OSA. The recorded data of AHI and AAI indexes from the portable SC-micro device may be valuable to determine and evaluate in an uncomplicated patient with suspected OSA. HSAT devices are reliable, comfortable, easy to use, and cost-effective. More extensive scientific research needed to understand the effects of AAI in arousal . We think that the use of HSAT devices should be encouraged in the rapid screening of OSA patients, since they are a practical and inexpensive scanning method.

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